

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number : 064179

**Trade Name :CYCLOSPIRINE USP (NON STERILE
BULK)**

Generic Name: Cyclosporine USP (Non sterile Bulk)

Sponsor : AAC Consulting Group, Inc.

Approval Date: July 2, 1997

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION **064179**

CONTENTS

	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
Tentative Approval Letter				
Approvable Letter				
Final Printed Labeling				
Medical Review(s)				
Chemistry Review(s)	X			
EA/FONSI				
Pharmacology Review(s)				
Statistical Review(s)				
Microbiology Review(s)				
Clinical Pharmacology				
Biopharmaceutics Review(s)				
Bioequivalence Review(s)				
Administrative Document(s)				
Correspondence				

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 064179

APPROVAL LETTER

JUL 2 1997

AAC Consulting Group, Inc.
U.S. Agent for: Sicor S.p.A.
Attention: Anthony C. Celeste
7475 Wisconsin Avenue, Suite 850
Bethesda, MD 20814

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Dear Sir:

This is in reference to your abbreviated antibiotic drug application dated May 7, 1996, submitted pursuant to Section 507 of the Federal Food, Drug, and Cosmetic Act, for Cyclosporine, USP (non-sterile bulk).

Reference is also made to your amendments dated January 24, and June 9, 1997.

We have completed the review of this abbreviated application and have concluded that the drug is acceptable for manufacturing, processing or repacking, as defined in this application. Accordingly, the application is approved.

Under 21 CFR 314.70, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.81. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Sincerely yours,

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER **074637**

CHEMISTRY REVIEW(S)

1. CHEMISTRY REVIEW NO. 3

2. ANDA # 64-179

3. NAME AND ADDRESS OF APPLICANT

AAC Consulting Group, Inc.
Attention: Anthony C. Celeste
U.S. Agents for: SICOR S.p.A.
7475 Wisconsin Avenue, Suite 850
Bethesda, MD 20814

4. LEGAL BASIS FOR SUBMISSION 21 CFR 430.4(a)(51), 448.23.

Part of the basis for a refuse to file was the fact that the organism used in this application is not one of the organisms listed in the regulation for the definition of cyclosporine. Data is provided by the applicant to establish chemical equivalence to the substance produced by the innovator using the listed organisms. The organism used in this application is *Cordyceps militaris*. The applicant provided a petition for including *Cordyceps militaris* on the list of organisms in the regulatory definition for cyclosporine, 21 CFR 430.4(a)(51).

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME N/A

7. NONPROPRIETARY NAME

Cyclosporine USP

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:

May 7, 1996	Date of application
June 18, 1996	Refuse to file letter
August 1, 1996	Amendment
November 8, 1996	N/A letter
January 24, 1997	Amendment
May 29, 1997	Facsimile deficiency
Undated	Amendment (hand delivered 6-13-97)

10. PHARMACOLOGICAL CATEGORY

Immunosuppressive agent for the prophylaxis of organ rejection in allogeneic transplants.

11. Rx or OTC Rx

12. RELATED IND/NDA/DMF(s) See section "37." Of this review.

13. DOSAGE FORM bulk

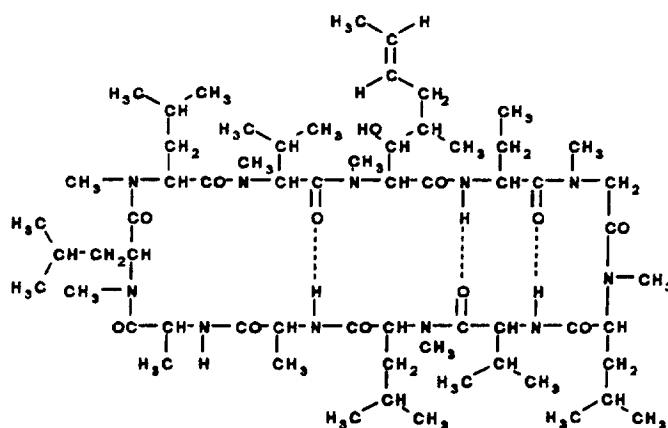
14. POTENCY bulk

15. CHEMICAL NAME AND STRUCTURE

Cyclosporine USP; $C_{62}H_{111}N_{11}O_{12}$;
M.W. = 1202.64

[R[R*,R*-(E)]]-Cyclic(L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl-3-hydroxy-N,4-dimethyl-L-2-amino-6-octenoyl-L- α -aminobutyryl-N-methylglycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl).

CAS [59865-13-3]



15. CHEMICAL NAME AND STRUCTURE (continued)

The organism used in this application is *Cordyceps militaris*. This organism is not one of those listed in the regulation defining Cyclosporine. Data are provided by Sicor to establish chemical equivalence to the substance produced by the innovator using one of the listed organisms.

Sicor provides ¹H NMR, ¹³C NMR, Mass Spectrum, and IR data. The data indicate that the product of the process described in this application is the same as the Cyclosporine USP reference standard.

16. RECORDS AND REPORTS N/A17. COMMENTS

Previous CMC concern The deficiency from the previous May 29, 1997, facsimile deficiency letter is copied, in *small italics*, followed by a review of the firm's undated response hand delivered 6-13-97:

(b)4 - Confidential Business

The COA format is revised to include the requested information. The COAs from the three exhibit batches are provided and they include the requested information.

18. CONCLUSIONS AND RECOMMENDATIONS Approve AADA 64-17919. REVIEWER: Jon E. ClarkDATE COMPLETED: June 16, 1997